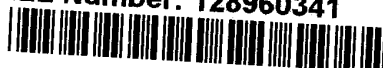


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Pharmaceuticals, Personal Care Products, and Endocrine Disruptors in Water: Implications for the Water Industry

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ABSTRACT

For over 70 years, scientists have reported that certain synthetic and natural compounds could mimic natural hormones in the endocrine systems of animals. These substances are now collectively known as endocrine-disrupting compounds (EDCs), and have been linked to a variety of adverse effects in both humans and wildlife. More recently, pharmaceuticals and personal care products (PPCPs) have been discovered in various surface and ground waters, some of which have been linked to ecological impacts at trace concentrations. The majority of EDCs and PPCPs are more polar than traditional contaminants and several have acidic or basic functional groups. These properties, coupled with occurrence at trace levels (i.e., <1 µg/L), create unique challenges for both removal processes and analytical detection. Reports of EDCs and PPCPs in water have raised substantial concern among the public and regulatory agencies; however, very little is known about the fate of these compounds during drinking and wastewater treatment. Numerous studies have shown that conventional drinking and wastewater treatment plants can not completely remove many EDCs and PPCPs. Oxidation with chlorine and ozone can result in transformation of some compounds with reactive functional groups under the conditions employed in water and wastewater treatment plants. Advanced treatment technologies, such as activated carbon and reverse osmosis, appear viable for the removal of many trace contaminants including EDCs and PPCPs. Future research needs include more detailed fate and transport data, standardized analytical methodology, predictive models, removal kinetics, and determination of the toxicological relevance of trace levels of EDCs and PPCPs in water.

Key words: endocrine disruptor; pharmaceutical; drinking water; wastewater; treatment; review

ENDOCRINE DISRUPTING COMPOUNDS

PERHAPS THE MOST DIFFICULT PART of understanding the subject of endocrine disruption involves a definition

of the term. The Environmental Protection Agency (EPA) has defined environmental endocrine disrupting compounds (EDCs) as exogenous agents that interfere with the "synthesis, secretion, transport, binding, action, or elimi-

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nation of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and/or behavior" (EPA, 1997). However, definitions and opinions on what defines an EDC vary greatly. It is generally accepted that the three major classes of endocrine disruption endpoints are estrogenic (compounds that mimic or block natural estrogen), androgenic (compounds that mimic or block natural testosterone), and thyroidal (compounds with direct or indirect impacts to the thyroid). As we will illustrate, the majority of research thus far has focused only on estrogenic compounds; however, disruption of androgen and thyroid function may be of greater or equal importance biologically.

Although the topic of endocrine disruption is considered an "emerging issue" in the water industry, scientists have known about the ability of natural and synthetic compounds to interfere with the hormone systems of animals for over 70 years. The discovery that certain compounds can mimic the endogenous hormones of animals was reported as early as the 1930s (Cook *et al.*, 1934; Walker and Janney, 1930). In 1940, Stroud reported that certain synthetic chemicals were estrogenic (Stroud, 1940). An article from the journal *Science* published in 1946 explained that the molecular configurations of natural and

synthetic compounds influenced the degree of estrogenic and androgenic bioactivity in rodents (Schueler, 1946). The ability of estrogenic and androgenic compounds to interfere with the natural metamorphosis of amphibians was reported as early as 1948 (Sluczewski and Roth, 1948). These early papers began to describe how the molecular configurations of natural and synthetic compounds could mimic the primary endogenous female hormone 17 β -estradiol (E2) and the male hormone testosterone. More importantly, these early studies laid the foundation for how these hormone-mimicking compounds could result in reproductive toxicity. Figure 1 provides the structures for some estrogenic compounds.

The estrogenic activity of synthetic organic compounds was of little interest to the environmental community until the discovery that the organochlorine pesticide, DDT and its metabolites had endocrine-disrupting properties (Fisher *et al.*, 1952; Bitman *et al.*, 1968; Welch *et al.*, 1969; Bitman and Cecil, 1970; Wrenn *et al.*, 1970). The connection between endocrine disruption and reproductive failures in wildlife was not made until the 1980s, when it was reported that gulls living in areas contaminated with DDT exhibited deformed sex organs and skewed sex ratios (Fry and Toone, 1981; Fry *et al.*, 1987). This was one of the first docu-

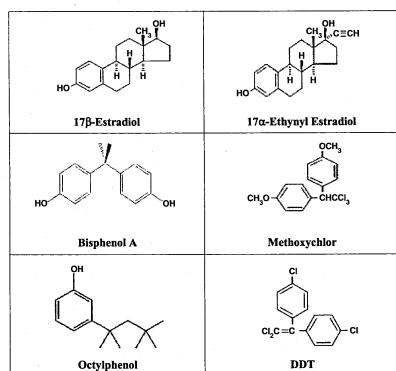


Figure 1. Structures of estrogenic compounds.

mented connections between an environmental contaminant and reproductive impacts via a hormone-mediated mechanism. Possible links between organochlorine pesticides, including DDT and its metabolites, and endocrine disruption were provided by researchers in Florida, who discovered reproductive disorders in alligators in Lake Apopka (Guillette *et al.*, 1994, 1996).

More recent studies have further demonstrated the importance of endocrine disruption in wildlife populations. For example, marine gastropods exposed to tributyltins, which leach from certain antifouling paints and PVC pipes, experienced severe population declines and reproductive disorders including imposex (development of male sex characteristics in females) (Gibbs *et al.*, 1991). In some amphibian populations, supernumerary limbs and missing limbs have been attributed to certain pesticides and other anthropogenic chemicals (Ouellet *et al.*, 1997; Sparling, 2000). In particular, trace concentrations of the widely used herbicide atrazine have been associated with endocrine disruption in frogs from the Midwestern United States (Hayes *et al.*, 2002). Degradation products from the widely used alkylphenol polyethoxylate (APE) surfactants, which are ubiquitous contaminants of wastewater treatment plant effluents, have been shown to be estrogenic (Mueller and Kim 1978; White *et al.*, 1994; Routledge and Sumpter 1997; Giesy *et al.*, 2000) and bioaccumulative (Abel *et al.*, 1993; Liber *et al.*, 1999; Lye *et al.*, 1999; Snyder *et al.*, 2001a). In the 1990s, reports from the United Kingdom and the United States indicated that fish living below wastewater treatment plants had several reproductive abnormalities (Bevans *et al.*, 1996; Folmar *et al.*, 1996; Harries *et al.*, 1996; Purdom *et al.*, 1994; Jobling *et al.*, 1998). These reproductive abnormalities included changes in the levels of sex steroids, gonadal histology (e.g., hermaphroditism and intersex), and increased levels of the female egg yolk precursor, vitellogenin, in male fish. Collectively, these impacts of wastewater effluent on male fish are referred to as feminization because fish that are genetically male exhibit female sex characteristics. However, conclusive data linking population level impacts on fish from EDC exposures has not yet been published. There are many other examples of exogenous compounds acting as EDCs, and more EDCs will likely be discovered as screening and testing methods become available.

Endocrine disruption also can be caused by naturally occurring compounds. For example, estrogens from plant sources, known as phytoestrogens, have been linked to reproductive failures in animals since the 1930s (Walker and Janney, 1930; Levin *et al.*, 1951; Brookbanks *et al.*, 1969; Metzler and Pfeiffer, 1995; Safe and Gaido, 1998). This effect was evident in sheep grazing on certain strains of clover in New Zealand. These sheep exhibited severe

reproductive impairment due to phytoestrogens (Millington *et al.*, 1964; Adams, 1998). Likewise, the inability of captive cheetahs to reproduce at the Cincinnati Zoo was linked to a diet high in phytoestrogens (Setchell *et al.*, 1987). In 1951, a vegetable oil was found to contain various phytoestrogens and phytoandrogens (Levin *et al.*, 1951). Interestingly, various over-the-counter medicinal supplements, such as those recommended for estrogen replacement therapy in postmenopausal women, contain high levels of phytoestrogens. Research is necessary to assess the relative importance of phytoestrogens in human diet, both by direct ingestion of vegetables and vegetable products and possibly from bioaccumulation of phytoestrogens in meat products. Likewise, industrial activities that release large quantities of phytoestrogens may have adverse effects on aquatic ecosystems as evidenced by recent studies documenting masculinization of fish exposed to effluent from pulp and paper mills and the presence of androgenic compounds in these effluents (Munkittrick *et al.*, 1997; Bortone and Cody, 1999; Larsson *et al.*, 2000; Jenkins *et al.*, 2001). Likewise, the degradation of vegetable matter and paper products in wastewater treatment plants (WWTPs) may contribute to releases of phytoestrogens into the aquatic ecosystem.

Initial attempts to identify the cause of feminization of fish exposed to wastewater effluent focused on synthetic organic chemicals with known estrogenic effects, such as plasticizers and APE surfactant degradation products. However, a series of studies employing *in vitro* bioassay-directed chemical fractionation implicated the human hormone, 17 β -estradiol (E2), and the synthetic birth control pharmaceutical, 17 α -ethinyl estradiol (EE2), as the most potent estrogens in these complex mixtures (Desbrow *et al.*, 1998; Snyder *et al.*, 1999, 2001c). Related research involving exposure of fish to E2 and EE2 under laboratory conditions at concentrations as low as 2 ng/L could induce measurable changes in fish reproduction (Arcand-Hoy *et al.*, 1998; Kramer *et al.*, 1998; Panter *et al.*, 1998; Routledge *et al.*, 1998). These reports indicated that a pharmaceutical (EE2) could induce endocrine-disruptive effects in fish at concentrations present in some municipal WWTP effluents. This cause-effect relationship has stimulated a great deal of new research on the identification of trace pharmaceuticals in the environment.

The unexpected impacts of trace concentrations of EDCs on wildlife raised concerns about the potential effects of these chemicals on humans (Colborn *et al.*, 1997). The best documented instance of endocrine disruption in humans involved *in utero* exposure to the potent synthetic estrogen diethylstilbestrol (DES), which resulted in adverse reproductive impacts in human offspring (Herbst *et al.*, 1971; Gill *et al.*, 1979). In this case, DES exposure

was not as an environmental contaminant; it was used as a pharmaceutical administered to pregnant women (Sower *et al.*, 1983; Rumsey and Hammond, 1990). However, the unanticipated sensitivity of the developing human reproductive system to DES clearly demonstrates that the human embryo/fetus is not immune to insult by exogenous chemicals that act as hormones. Besides use as a human pharmaceutical, DES is also used for certain agricultural applications such as increasing livestock growth and milk production.

Some researchers have attributed decreases in human sperm quality and quantity over the past 5 decades to endocrine disrupting compounds in the environment (Sharpe and Skakkebaek, 1993; Stone, 1994; Carlsen *et al.*, 1995). Likewise, it has been suggested that sharp increases in breast, testicular, and prostate cancers reported over the past 40 years are related to endocrine disrupting compounds in the environment (Krishnan and Safe, 1993; Ahlborg *et al.*, 1995; Carlsen *et al.*, 1995; Ashby, 1997; EPA, 1997; Gillesby and Zacharewski, 1998). However, this topic is still quite controversial, and other scientists have produced data refuting these arguments. If EDCs are causing adverse human health effects, it is unlikely that these effects would be caused by estrogenic chemicals in water due to their extremely minute concentrations that result in doses that are small compared to phytoestrogens and other estrogenic compounds present in food sources. Estrogenic hormones in water are less likely to cause adverse effects in humans than they are in fish due to differences in exposures. Although fish may be constantly exposed to EDCs present in the aquatic environment, humans are exposed mainly through ingestion of limited quantities of water.

In addition to compounds capable of eliciting estrogenic activity, concerns have been raised regarding human health effects associated with pollutants that interact with other hormone systems. Recently, a great deal of public and regulatory interest has focused on perchlorate (ClO_4^-), which affects the thyroid gland by competitively inhibiting iodide transport (Urbansky, 2000; Logan, 2001). Ammonium perchlorate is a strong oxidizer that has been used extensively in solid-rocket fuels, fireworks, matches, and other industrial and domestic uses (Urbansky, 2000). Nearly every state in the United States has known perchlorate use, storage, or manufacturing sites, and perchlorate contamination has recently been found in many ground and surface waters (Wang *et al.*, 2002). Perchlorate salts were also used as a pharmaceutical to treat overactive thyroid disease and continue to be used to treat side effects of certain chemotherapy drugs (Wang *et al.*, 2002). Because perchlorate has a direct impact on the thyroid, it is considered an EDC, and will likely become the first drinking water

contaminant regulated on endocrine disrupting toxicity, as the U.S. EPA is currently establishing a reference dose.

Some scientists have suggested that some drinking water disinfection byproducts (DBPs) may act as EDCs. Several reports, which include epidemiological studies, have reported increases in spontaneous abortions and cancers in humans as linked to elevated concentrations of halogenated disinfection byproducts (King and Marrett, 1996; King *et al.*, 2000a, 2000b). Additionally, the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), a Federal Advisory Committee, suggested that DBPs should be included among the mixtures to be evaluated for endocrine disruptive effects (EPA, 1998). Because DBPs generally are orders of magnitude greater in concentration than EDCs and pharmaceutical and personal care products (PPCPs), and have been implicated as human reproductive toxicants, efforts to control EDCs and PPCPs by oxidation ultimately may prove to be counterproductive due to increased byproduct formation potential.

PHARMACEUTICALS AND PERSONAL CARE PRODUCTS (PPCPs)

The first concerns regarding potential adverse effects of pharmaceuticals in municipal wastewater were expressed by Stumm-Zollinger and Fair in 1965 and Tabak and Bunch in 1970 (Stumm-Zollinger and Fair, 1965; Tabak and Bunch, 1970). In their visionary, but largely forgotten study of the biotransformation of estrogenic hormones by activated sludge, they noted that natural and synthetic estrogens could pose an ecological threat. Other studies conducted in the United States during the 1970s documented the presence of other pharmaceuticals, such as clofibrate and salicylic acid in wastewater effluents (Garrison *et al.*, 1975; Hignite and Azamoff, 1977). Later studies have shown that natural and synthetic estrogens are ubiquitous contaminants of wastewater at trace concentrations (Tabak *et al.*, 1981; Aherne *et al.*, 1985; Desbrow *et al.*, 1998; Lee and Peart, 1998; Snyder *et al.*, 1999; Huang and Sedlak, 2001). However, reports demonstrating the possible impacts of trace levels (ng/L) of the pharmaceutical EE2 (Arcand-Hoy *et al.*, 1998; Desbrow *et al.*, 1989; Renner, 1998; Snyder *et al.*, 2001c) have stimulated a dramatic increase in research on these compounds as environmental contaminants (Halling-Sorensen *et al.*, 1998; Daughton and Ternes, 1999; Snyder *et al.*, 2001a). A wide variety of PPCPs have now been reported as environmental contaminants including antibiotics, X-ray contrast media, analgesics, antiseptics, and many others (Halling-Sorensen *et al.*, 1998; Daughton and Ternes, 1999). In the United States,

a recent survey indicated widespread PPCP contamination of streams (Kolpin *et al.*, 2002). Table 1 shows several of the most frequently detected EDCs and PPCPs along with concentration, usage, and structural information. Unfortunately, sparse data exist to explain the toxicological relevance of trace pharmaceutical compounds. Nevertheless, public perception regarding the presence of PPCPs in water supplies has increased attention to this issue despite the very low concentrations reported.

U.S. REGULATORY ISSUES

In the United States, regulation of contaminants in drinking water began in 1962, with the Public Health Services Standards. These regulations included several compounds now known to be endocrine disruptors, such as arsenic, cadmium, and some phenols. The Safe Drinking Water Act of 1974 is the principal law governing drinking water safety in the United States. This law required the EPA to establish maximum contaminant levels for various drinking water contaminants including some pesticides now known to have endocrine-disruptive activity. However, endocrine disruption was not specifically named in any United States legislation until 1995 with amendments to the Safe Drinking Water Act (bill number S.1316) and Food Quality Protection Act (bill number P.L. 104-170), mandating that chemicals and formulations be screened for potential endocrine activity before they are manufactured or used in certain processes where drinking water and/or food could become contaminated. Under these laws, the EPA is required to "develop a screening program, using appropriate validated test systems and other scientifically relevant information, to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effect as the Administrator may designate." Furthermore, these laws specify that the EPA must have developed a testing program by 1998, implemented the program by 1999, and reported to Congress by 2000.

Table 1. Compounds with highest frequency of detection in recent USGS EDC/PPCP survey of U.S. streams (Kolpin *et al.*, 2002).

Compounds	Use	Frequency of detection (%)	LogKow, measured (calculated)
Coprostanol	Estrogen	~80%	(8.82)
Cholesterol	Plant/animal steroid	~80%	(8.74)
N,N-diethyltoluamide	Mosquito repellent	~80%	2.18 (2.26)
Caffeine	Stimulant	~75%	-0.07 (0.16)
Tris (2-chloroethyl)phosphate	Fire retardant	~75%	1.44 (1.63)
Triclosan	Antibiotic	~60%	NA
4-Nonylphenol	Surfactant	~60%	(5.92)
4-Nonylphenol monoethoxylate	Surfactant	~50%	NA
Ethanol, 2-butoxy-phosphate	Plasticizer	~45%	NA
4-Octylphenol monoethoxylate	Surfactant	~45%	NA
Bisphenol A	Plasticizer	~45%	3.32 (3.64)
Cotinine	Nicotine metabolite	~35%	0.07 (0.34)
4-Nonylphenol diethoxylate	Surfactant	~35%	NA
5-Methyl-1H-benzotriazole	Antioxidant	~30%	NA
Fluoranthene	PAH	~30%	5.16 (4.93)
1,7-Dimethylxanthine	Caffeine metabolite	~30%	-0.22 (-0.39)
Pyrene	PAH	~25%	4.88 (4.93)
Trimethoprim	Antibiotic	~25%	NA
1,4-Dichlorobenzene	Deodorizer	~25%	3.44 (3.28)
Acetaminophen	Analgesic	~25%	0.46 (0.27)
Tetrachloroethylene	Solvent	~20%	NA
4-Octylphenol diethoxylate	Surfactant	~20%	NA
Erythromycin-H ₂ O	Antibiotic	~20%	NA
Estriol	Estrogen	~20%	2.45 (2.81)
Lincomycin	Antibiotic	~15%	0.59 (0.29)
Sulfamethoxazole	Antibiotic	~15%	0.89 (0.48)
Phthalic anhydride	Plasticizer	~15%	1.60 (2.07)
Carbaryl	Insecticide	~15%	NA

To meet the requirements of this recent legislation, the EPA formed the EDSTAC to provide recommendations on a conceptual framework, priority setting, screening, and testing methodologies, and communication and outreach programs. The EDSTAC group consisted of various stakeholders and experts in reproductive toxicology. The committee began deliberations in October of 1996 and issued a final report in July of 1998 recommending that human and wildlife impacts be considered, and that estrogen, androgen, and thyroid (EAT) end points be examined (EPA, 1998). The conceptual framework devised by EDSTAC consists of an initial sorting, prioritization, Tier 1 and 2 testing, and a hazard assessment of an estimated 87,000 chemicals. In addition to discrete chemicals, EDSTAC recommended the evaluation of mixtures of chemicals in breast milk, baby formulas, hazardous waste sites, pesticides and fertilizers, drinking water DBPs, and gasoline.

In 2001, the EPA formed the Endocrine Disruptor Methods Validation Subcommittee (EDMVS) to evaluate the test battery suggested by EDSTAC. The EDMVS is tasked with method validation by determining if a particular method is transferable to other laboratories, can be validated with representative chemicals, has sufficient sensitivity to EAT end points, and has appropriate standard operating procedures. Some difficult issues encountered in the standardization of EDC testing include animal diets, dosing methods and ranges, testing of mixtures, and interspecies comparisons. The outcome of this screening battery is critical to the water industry, as it is designed to definitively identify EDCs. However, it is important to note that the current legislation regulates only the industries producing or using raw chemicals, and not the water industry. As a result, these actions may have little immediate effect on water and wastewater treatment regulations.

There are currently no federal regulations for pharmaceuticals in drinking or natural waters. The Food and Drug Administration (FDA) requires ecological testing and evaluation of a pharmaceutical only if an environmental concentration in water or soil is expected to exceed 1 $\mu\text{g/L}$ or 100 $\mu\text{g/kg}$, respectively (FDA, 1998). In light of the recent data on the occurrence of PPCPs in the aquatic environment, these policies may need to be reconsidered. Although extensive monitoring programs are underway, toxicological studies conducted at environmentally relevant concentrations are necessary for intelligible regulations to be established. The State of California has been considering the potential impacts of EDCs and PPCPs, especially when municipal wastewater effluent is used for indirect potable reuse. A recent modification to California's draft regulations for indirect potable reuse states, "Each year, the PGRRP [planned

groundwater recharge reuse project] shall monitor the recycled water for endocrine disrupting chemicals and pharmaceuticals specified by the Department, based on a review of the PGRRP engineering report and the affected groundwater basin(s)." Although the regulations have not been finalized, many practitioners of indirect potable reuse in California are establishing monitoring programs for EDCs and PPCPs. Because California's water reuse program often establishes precedents for programs throughout the world, it is likely that other regulatory agencies will adopt similar language in their own water recycling programs.

ANALYTICAL METHODS

Because EDCs represent a broad variety of compounds, it is important to define which EDCs one seeks to analyze. It is widely accepted that DDT and other organochlorine pesticides can act as EDCs. Methodologies for these "classic" contaminants, as well as various endocrine-disrupting metals, are well established with standardized protocols used in drinking and wastewater regulations. The majority of novel analytical work is focused on trace levels of less-characterized contaminants with greater polarity than many of the "classic" contaminants. Several classes of EDCs and PPCPs have acidic or basic moieties, large molecular weights, and/or polar functional groups. No standard methods are currently available for these compounds, and few commercial laboratories analyze these compounds. A further complication is the desire to quantitate these compounds at ultratrace concentrations (sub-ng/L), which may have toxicological relevance (e.g., EE2).

A vast array of analytical methodologies has been applied for the quantitation of EDCs and PPCPs in water. Although direct measurement is possible (Yoon et al., 2003), the majority of methods involve an extraction procedure followed by instrumental and/or immunoassay analyses (Tabak and Bunch, 1970; Keith et al., 1975; Hignite and Azarnoff, 1977; Ahern et al., 1985; Shore et al., 1993; Ternes et al., 1998; Snyder et al., 1999, 2001a; Stumpf et al., 1999; Heberer and Dumbier, 2000; Huang and Sedlak, 2001). The type of extraction, volume of water used, and type of analytical equipment used depend on the compounds to be analyzed and source of water. For instance, WWTP effluents are the major source of these compounds to surface waters. The analysis of WWTP effluents provides unique challenges for trace quantification because the effluent also contains numerous interfering compounds associated with organic matter. Consequently, extensive extraction, cleanup, and sophisticated instrumentation usually is required to ana-

lyze these compounds. Several methodologies for quantitation of EDCs and PPCPs in natural waters used solid-phase extractions followed by instrumental analyses using gas chromatography coupled with mass spectrometric detection, liquid chromatography with mass spectrometric detection, immunoassays, or a combination of techniques (Keith et al., 1975; Hignite and Azarnoff, 1977; Tabak et al., 1981; Ahern et al., 1985; Shore et al., 1993; Ternes et al., 1998; Snyder et al., 1999, 2001a; Stumpf et al., 1999; Heberer and Dumbier, 2000; Huang and Sedlak, 2001; Ternes, 2001). Each method has advantages and disadvantages, detailed descriptions of which are outside the scope of this paper.

Bioanalytical techniques are important tools for monitoring certain EDCs and PPCPs. These techniques employ a biological end point that is related to a type of toxicity or a class of compounds. The most simple methods are receptor binding assays and cellular bioassays that have rapid response times, high sensitivity, and relatively low cost (Welch et al., 1969; Mueller and Kim, 1978; Anderson et al., 1996; Routledge and Sumpter, 1997; Zacharewski, 1997; Snyder et al., 2000, 2001c). *In vivo* bioassays are also used to detect various classes of EDCs. The most common biomarker for estrogenic exposure in the aquatic environment is an increase in plasma vitellogenin (an egg yolk lipid) in male fish. Fish can be caged in various susceptible waters and tested for various endocrine biomarkers to determine the extent of EDC exposure. Several studies of this nature have found significant reproductive impacts in fish caged below wastewater outfalls (Purdum et al., 1994; Rudel, 1997; Routledge et al., 1998; Miles-Richardson et al., 1999; Snyder et al., 2000). Although each instrumental and bioanalytical technique has advantages and disadvantages, a combination of these methods is most likely to detect and quantify EDCs. This approach is often referred to as toxicity identification evaluation, and may use bioassay-directed fractionation to guide instrumental analyses towards elucidation of toxic compounds (Deshrow et al., 1998; Routledge et al., 1998; Castillo and Barcelo, 1999; Snyder et al., 2001c). The issue of mixture toxicity, especially in relation to endocrine disruption, may likely drive the drinking water industry to employ a number of biological monitoring tools. Since all environmental contaminants exist as components of complex mixtures, biological tests may be the only way to assess the total endocrine-disruptive potential of contaminants in water.

EDC/PPCP removal during water treatment

EDCs and PPCPs in municipal wastewater can be removed during wastewater treatment, during their passage through surface or groundwater (e.g., natural at-

tenuation) or during drinking water treatment. To assess the potential for exposure of humans and aquatic organisms to these compounds and to design more effective treatment systems, environmental professionals need to understand the mechanisms through which EDCs and PPCPs are attenuated in engineered and natural systems. The best understood of the treatment processes is conventional wastewater treatment (Ternes, 1998; Ternes et al., 1999a, 1999b; Johnson and Sumpter, 2001). Compared to municipal wastewater treatment plants, much less is known about the behavior of EDCs and PPCPs in receiving waters and in drinking water treatment plants. Therefore, the purpose of this review is to summarize existing data, to predict the behavior of different classes of EDCs and PPCPs based upon chemical properties, and to identify areas where additional research is needed.

Conventional surface water treatment plants (SWTPs) typically treat water via coagulation using alum, ferric chloride, and/or synthetic polymers followed by flocculation, sedimentation, filtration, and disinfection. Conventional SWTPs achieve high removals of pathogens and other biological particles, and modest removal of dissolved organic carbon (DOC, 1 to 10 mg/L). In the United States, chlorine and chloramines are typically used for disinfection, while ozonation is more commonly practiced in European countries. Alternative SWTP designs or modifications to conventional WTPs sometimes include additional water treatment processes (e.g., activated carbon, biofiltration, membranes, aeration, chemical softening, ultraviolet light irradiation).

Our understanding of the removal of EDCs and PPCPs in receiving waters and in drinking water treatment systems is limited because the analyses for these compounds are rare, and when detected, they are present at fluctuating concentrations near analytical method detection limits. With a few notable exceptions, most of our knowledge about the removal of these compounds is derived from laboratory or bench-scale studies. When data on removal of EDCs and PPCPs are not available, it may be possible to make predictions based upon results of previous research with contaminants exhibiting similar chemical properties.

As a result of much evidence linking estrogenic hormones to endocrine disruption in fish, there has been a great deal of interest in the fate of E2, EE2, and nonylphenol ethoxylates (NPEs) in surface waters. For example, laboratory studies designed to simulate microbial transformation of NPEs in surface waters indicate that they are degraded in 4 days (Mann and Boddy, 2000), which is consistent with the observation of a relatively small decrease in concentrations when nitrified wastewater effluent passes through an engineered treatment wetland.

Studies conducted at a drinking water treatment plant along the Severn Trent Region, a system with significant inputs of wastewater effluent, indicate that estrogenic hormones and other compounds capable of producing estrogenic effects in bioassays are removed during drinking water treatment (Fawell *et al.*, 2001).

The attenuation of PPCPs in receiving waters and in drinking water treatment plants also has been demonstrated in several studies and has been reviewed recently (Heberer, 2002). For example, the attenuation of several PPCPs was observed as secondary wastewater effluent was infiltrated into groundwater (Drewes *et al.*, 2001a) and during river bank filtration (Heberer, 2002). However, certain compounds, such as the iodinated X-ray contrast media were not removed during groundwater infiltration (Putschew *et al.*, 2000). In contrast to the efficient removal of many PPCPs observed in saturated and unsaturated groundwater, conventional drinking water treatment plants do not appear to remove PPCPs well. For example, clofibric acid has been detected at concentrations as high as 270 ng/L in drinking water from Berlin (Heberer and Dumbier, 2000). Of 47 wastewater tracers and EDCs analyzed, 15 were detected in raw drinking water (river water) samples, and 14 in finished drinking water samples from Atlanta (Henderson *et al.*, 2001). In that study, caffeine was present in all raw waters and some finished waters. Although all at trace concentra-

tions (ng/L), the following compounds were detected in finished drinking waters: tri(2-chloroethyl)phosphate, phthalic anhydride, triclosan, fluorethane, pyrene, 2,6-di-*t*-butylphenol, thanol-2-butoxy-phosphate, and tributyl phosphate. Caffeine, cotinine, and acetaminophen were also detected in the finished drinking water (Henderson *et al.*, 2001).

Although monitoring studies involving low concentrations of EDCs and PPCPs provide insight into the occurrence of these compounds in the environment, previously discussed issues associated with method detection limits and dilution factors complicate the analysis of monitoring data. As a result, more insight into removal processes can be obtained by examining specific treatment processes. Table 2 represents anticipated performance of different unit processes based upon literature reports with specific classes of compounds or compounds with similarities to other trace pollutants that have been studied in more detail. The following sections describe the potential for common water treatment processes to remove EDCs or PPCPs.

Chemical precipitation processes

Metal salts (aluminum sulfate, ferric chloride) and softening chemicals (calcium oxide, sodium carbonate) are commonly added to destabilize particles present in

water or to precipitate new particles (coagulation), aggregate particles (flocculation), and improve settling characteristics of particles (clarification). Sand filtration is commonly used after clarification for additional particle removal. Natural organic matter (NOM) and EDCs or PPCPs may adsorb to particles in water and metal hydroxide particles formed during coagulation. Furthermore, chemical precipitation can remove moderately hydrophobic organic contaminants that have a strong affinity for adsorbed NOM (Rebhun and Lurie, 1993). However, very little is known about the association of EDCs or PPCPs to particles present in water treatment systems. Therefore, it is difficult to make *a priori* predictions about the removal of EDCs or PPCPs during chemical precipitation processes.

Despite these potential shortcomings, considerable insight can be obtained by considering the behavior of pesticides, herbicides, and polycyclic aromatic hydrocarbons (PAHs) during chemical precipitation processes (Eldib and Aly, 1977; Rebhun *et al.*, 1998). Partitioning of organic compounds onto particles can occur through several mechanisms. For hydrophobic compounds, partitioning can be predicted from octanol-water partition coefficients (K_{OW}) (Karickhoff and Morris, 1985; Chiou *et al.*, 1998). Under the conditions encountered during water treatment, only those compounds with relatively high K_{OW} values (i.e., $>10^3$) will be removed to an appreciable degree. As indicated in Table 1, most compounds of potential concern are relatively polar (log K_{OW} values less than 3) and as a result, only a few EDCs and PPCPs (e.g., nonylphenol, fluorethane, pyrene) are expected to be removed during chemical precipitation. Some of the more hydrophobic compounds are present in wastewater effluents, but may not occur in raw drinking water supplies (Henderson *et al.*, 2001). Some surfactants have relatively high K_{OW} values, but include both polar and nonpolar moieties. The partitioning of octylphenol in English river sediments was greatest to the clay and silt fraction of the sediments, suggesting a hydrophobic interaction with organic carbon as well as surface area associated with the clay and silt particles (Johnson *et al.*, 1998). As a result, only a few compounds (e.g., bisphenol A, EE2, octylphenol, PAHs) could be associated with organic phases of particles in drinking water treatment plants.

In addition to hydrophobic partitioning, organic contaminants can be adsorbed to particles by interactions of polar functional groups with charged particles and mineral surfaces by complexation or ion exchange. For example, the observed sorption of many polar veterinary pharmaceuticals (e.g., tetracycline) to soil and sediment is considerably stronger than predicted by hydrophobic interactions alone (Tolls, 2001). Such interactions could

be particularly important in drinking water treatment, where mineral oxides provide a relatively high density of surface functional groups that could interact with polar pharmaceuticals. For example, approximately 25% of the NPEs in groundwater were removed during coagulation with alum (Fielding *et al.*, 1998). Therefore, it is possible that some polar EDCs or PPCPs could be removed during coagulation.

Despite the predictions, available data from pilot and full-scale water treatment plants indicate that removal will be modest at best. Neither lime softening nor alum coagulation (conventional or enhanced dosages ranging from 6 to 18 mg/L) demonstrated atrazine removal (Zhang and Emary, 1999). Coagulation/flocculation/sedimentation with alum and iron salts or excess lime/soda ash softening did not result in significant removal of antibiotics (i.e., carbadox, sulfachlorpyridazine, sulfadimethoxine, sulfamerazine, sulfamethazine, sulfathiazole, and trimethoprim) (Adams *et al.*, 2002). In another study, ferric chloride precipitation did not remove several pharmaceuticals frequently detected in surface waters (diclofenac, carbamazepine, bezafibrate, and clofibric acid) (Sacher *et al.*, 2000). Certain pesticides were poorly removed by coagulation and ~50% of the PAHs pyrene, fluorethane, and anthracene were removed through hydrophobic interactions (Eldib and Aly, 1977; Rebhun *et al.*, 1998). On the basis of predictions of hydrophobic interactions and results of full-scale measurements, we conclude that EDCs and PPCPs not associated with colloidal or particulate material will most likely be poorly removed during coagulation.

Activated carbon adsorption

Activated carbon can be used to remove many different pesticides, pharmaceuticals, and estrogenic compounds (Robeck *et al.*, 1965; Steiner and Singley, 1979; Miltner *et al.*, 1989; Pirbazari *et al.*, 1992; Sacher *et al.*, 2000; West, 2000). The performance of activated carbon depends on the properties of the activated carbon sorbent (surface area, pore size distribution, surface charge, oxygen content) and on the properties of the solute (shape, size, charge, and hydrophobicity). Hydrophobic interactions are the dominant mechanism of removal for most organic compounds in activated carbon adsorption systems. However, ion exchange interactions can result in removal of polar solutes (Youssef *et al.*, 1982; Matsumura *et al.*, 1985; Crittenden *et al.*, 1999). As a result of the hydrophobic interactions, activated carbon efficiently removes most nonpolar organic compounds (i.e., those compounds with log $K_{OW} > 2$). The ability of activated carbon to remove more polar compounds will de-

Table 2. Unit processes and operations used for EDCs and PPCPs removal.

Group	Classification	AC	BAC	O ₃ /AOPs	UV	Cl ₂ /ClO ₂	Coagulation/ flocculation	Softening/ metal oxides	NF	RO	Degradation (B/P/AS) ^a
EDCs	Pesticides	E	E	L-E	E	P-E	P	G	G	E	E (P)
	Industrial chemicals	E	E	F-G	E	P	P-L	P-L	E	E	G-E (B)
	Steroids	E	E	E	E	E	P	P-L	G	E	L-E (B)
	Metals	G	G	P	P	P	F-G	F-G	G	E	P (B), E (AS)
	Inorganics	P-L	F	P	P	P	P	G	G	E	P-L
PhACs	Organometallics	G-E	G-E	L-E	F-G	P-F	P-L	P-L	G-E	E	L-E
	Antibiotics	F-G	E	L-E	F-G	P-G	P-L	P-L	E	E	E (B) G-E (P)
	Antidepressants	G-E	G-E	L-E	F-G	P-F	P-L	P-L	G-E	E	G-E
	Anti-inflammatory	E	G-E	E	E	P-F	P	P-L	G-E	E	E (B)
	Lipid regulators	E	E	E	F-G	P-F	P	P-L	G-E	E	P (B)
PCPs	X-ray contrast media	G-E	G-E	L-E	F-G	P-F	P-L	P-L	G-E	E	E (B and P)
	Psychiatric control	G-E	G-E	L-E	F-G	P-F	P-L	P-L	G-E	E	G-E
	Synthetic musks	G-E	G-E	L-E	E	P-F	P-L	P-L	G-E	E	E (B)
	Sunscreen	G-E	G-E	L-E	F-G	P-F	P-L	P-L	G-E	E	G-E
	Antimicrobials	G-E	G-E	L-E	F-G	P-F	P-L	P-L	G-E	E	F (P)
Surfactants/detergents		E	E	F-G	F-G	P	P-L	P-L	E	E	L-E (B)

^aB, biodegradation; P, photodegradation (solar); AS, activated sludge; E, excellent (>90%); G, good (70-90%); F, fair (40-70%); L, low (20-40%); P, poor (<20%).

pend upon the strength of the polar interactions, which are difficult to predict *a priori*.

NOM in water competes for adsorption sites and decreases the activated carbon capacity for micropollutants (Newcombe *et al.*, 1997a, 1997b; Pendleton *et al.*, 1997; Newcombe, 1999; Wu and Pendleton, 2001). As a result, treatability studies conducted in distilled water should be interpreted with caution because they do not consider competition from NOM. For example, addition of 10 to 20 mg/L of powdered activated carbon (PAC) to distilled and river water spiked with seven antibiotics achieved between 50% and greater than 99% removal. However, when the same experiments were repeated in river water containing 10.7 mg/L of NOM, removal decreased by 10 to 20% (Adams *et al.*, 2002).

Although results of full-scale treatment studies with EDCs and PPCPs are not available, considerable information is available on the ability of activated carbon to remove compounds that cause taste and odor problems. PAC is usually added in presedimentation or contact basins prior to coagulation, sedimentation, and filtration. Usually, 1 to 3 h of contact is provided for the PAC, after which the PAC settles out in the sedimentation tank, and is then disposed with other WTP sludges. For example, PAC added at dosages ranging from 5 to 50 mg/L removed greater than 90% of methylisoborneol (Log K_{OW} = 3.1) in raw water (Gilligly *et al.*, 1998; Zhang and Emery, 1999; Bruce *et al.*, 2002). Under the conditions encountered in drinking water treatment plants, removal of micropollutants by PAC tends to be independent of initial contaminant concentrations (Knappe *et al.*, 1998; Leung and Segar, 1999). In a laboratory, 20 mg/L of PAC with 1-h contact time reduced the concentration of the moderately hydrophobic pesticide lindane (Log K_{OW} = 3.72) from 10 to 0.1 μ g/L (Kouras *et al.*, 1998). Laboratory studies conducted with EDCs suggest that PAC will be effective at removing between approximately 60 and 80% of nonylphenol and NPEs (Carlile *et al.*, 1996; Fielding *et al.*, 1998). Unpublished PAC experiments in distilled water and/or surface water conducted by the authors suggest similar removals of E2, EE2, triclosan, dilantin, bisphenol A, and octylphenol.

Granular activated carbon (GAC) systems operate as adsorptive packed beds or filters. While PAC is added, contacted with water (~4 h), and removed (settling/filtration), GAC systems operate with stationary phase (GAC packed beds), continuous water flow, and contact times of less than 30 min. GAC systems remain in operation for months to years, and thus achieve pseudo-equilibrium with micropollutants in the influent water (Crittenden *et al.*, 1991). The influent micropollutant and DOC concentrations, contact time with the GAC, and

type of GAC impact the adsorption and breakthrough of the micropollutant across GAC systems. For example, the adsorption characteristics of three types of activated carbon for radiolabeled 17 β -estradiol were studied to determine the time necessary to reach equilibrium between the solid and the liquid phase (Fuerhacker *et al.*, 2001). 17 β -Estradiol was quickly adsorbed and conditions close to equilibrium were reached after 50–180 min. The equilibrium concentrations were calculated to be at 49–81% of the initial concentrations between 1 and 100 ng/L, with 0.51 ng/L remaining for a 1 ng/L initial concentration and between 5.9 and 14.6 ng/L for a 100 ng/L initial concentration. Wang and Lee (1997) determined GAC (coal base) design criteria to remove various micropollutants including organophosphorus, volatile organic chemicals, and phenol found in drinking water sources having different background DOC concentrations. It was found that sorption capacities of the micropollutants were reduced with increasing background DOC concentration due presumably to DOC pore blockage of the GAC and reduction of the surface area available for the adsorption of micropollutants. The results obtained from activated carbon filtration for the removal of nonylphenol showed that contact times of 4 days and 24 h and activated carbon dosages of 0.1 and 1 g/L could be obtained with nonylphenol total contaminant loadings up to 0.01 mg/g on saturation of the GAC (Tanghe and Verstraete, 2001). The influence of temperature (4 or 28°C) on nonylphenol adsorption on GAC was negligible and the sorption capacity of dissolved humic acids for nonylphenol was considerable at a nonylphenol concentration of 10 μ g/L.

The use of GAC leads to very high removal of micropollutants during the first weeks/months, but over time, more strongly adsorbable constituents can displace previously adsorbed compounds. The relative strength of adsorption is often characterized by Freundlich isotherm parameters (e.g., sorption capacity, K). Freundlich " K " values are available for numerous compounds regulated under the Safe Drinking Water Act (Speth and Adams, 1993; Speth and Milner, 1998), and correlated with physical properties of organic compounds (Crittenden *et al.*, 1999). Freundlich constants can be used to predict PAC and GAC performance (Knappe *et al.*, 1998; Najm *et al.*, 1991a, 1991b). Typically, when K values were greater than 200 the activated carbon process is considered technically and economically feasible. Although K values are not currently available for emerging EDCs and PPCPs, quantitative structure-activity relationship models could be used to estimate the values. Generally, compounds with log K_{OW} values > 2 have Freundlich K values > 200 and, therefore, many EDCs and PPCPs (Table 1) may be amenable to removal by PAC or GAC.

Oxidation processes

In water treatment systems, several of the commonly used disinfectants also can result in transformation of EDCs and PPCPs. In drinking water treatment systems, chlorine, chlorine dioxide, and ozone are frequently used while disinfection of wastewater effluent usually is limited to chlorine. Oxidation of EDCs and PPCPs is selective for certain chemical structures and functional groups. Among the three oxidants, ozone tends to be the most reactive; however, all three oxidants are strong electrophiles that exhibit similar trends of reactivity with organic compounds. As a result, certain generalizations can be observed in the reactivity of the oxidants (Hoigne and Bader, 1983a, 1983b, 1994; Hoigne *et al.*, 1985; Larson and Weber, 1994; Tratnyek and Hoigne, 1994; Gallard and von Gunten, 2002): (1) dissociated acidic compounds are more reactive than protonated forms (i.e., reactivity increases with pH), but nondissociated bases are more reactive when not protonated; (2) general order of reactivity from highest to lowest for aromatic or aliphatic compounds: thiols > amines > hydroxyl > carboxyl; and (3) aromatic compounds are more reactive than aliphatic compounds.

Chlorination. In the United States, free chlorine (i.e., HOCl and OCl⁻) is commonly used for disinfection and oxidation of reduced inorganic species such as Fe(II), Mn(II), and S(-II). In the presence of ammonia, free chlorine will produce chloramines, which tend to be less reactive than free chlorine (Weil and Morris, 1974). For example, the application of free chlorine resulted in the removal of >95% of the herbicide glyphosate in Ohio River water after 15 min while monochloramine did not remove any of the herbicide under similar conditions (Speth, 1993). The reduced reactivity of chloramine is particularly important in wastewater treatment plants because enough ammonia will be present to convert free chlorine into monochloramine in wastewater effluent that has not undergone nitrification.

Free chlorine reacts rapidly with phenolic compounds, mainly through the reaction between hypochlorous acid and the deprotonated phenolate anion (Faust and Hunter, 1967). The reaction results in sequential chlorine addition to the aromatic ring followed by ring cleavage. The reactivity of the phenolic functional group likely explains the transformation of estrogenic hormones and nonylphenol by chlorine observed in laboratory studies (West, 2000). However, these results conflict with findings in Japan that report chlorine as ineffective for the degradation of estrogens (Matsui and Takigami, 2000).

The transformation of several amine-containing antibiotics (Adams and Kuzhikannil, 2000; Huang *et al.*,

2001), diclofenac (Sedlak and Pinkston, 2001), and caffeine (Gould and Richards, 1984), was observed in laboratory experiments with chlorine. Additional studies are needed to assess the reactivity of compounds with other potentially reactive functional groups and the relative importance of these reactions under conditions used for disinfection of water and wastewater. In addition, the reactions between chlorine and EDCs and PPCPs necessitate quenching of chlorine in samples that may have a chlorine residual, especially when 24-h composite samples are collected. For example, chlorination (1 mg/L; pH = 7.5) removed >90% of seven amine-substituted antibiotics from river water within 40 min (Adams and Kuzhikannil, 2000). Therefore, careful attention must be directed at discerning removal by chlorine vs. removal from a quenching agent.

Chlorine dioxide. Chlorine dioxide (ClO₂) can oxidize herbicides, pesticides, and PAHs, and is generally a stronger and faster oxidant than free chlorine (Ravacha and Blits, 1985). Chlorine dioxide application (1–1.5 mg/L for 10 min) at two full-scale WTPs removed less than 30% of the total pesticide concentration (0.05 to 3.5 μ g/L) in the raw water (Griffini *et al.*, 1999). ClO₂ was more effective than free chlorine at oxidizing amine-containing pesticides (phenylamide) and herbicides (ametryn) than for other herbicides (isoproturon, glyphosate) (Eldib and Aly, 1977; Speth, 1993; Lopez *et al.*, 1997). Chlorine dioxide (2 mg/L at pH 7) removed 50% of several PAHs, but contact times required for this level of oxidation ranged between 6 s (benzo[a]pyrene) to 17 h (benzo[b]fluoranthene) for different PAHs (Ravacha and Blits, 1985). No additional information is available on oxidation of EDCs or PPCPs by ClO₂. However, we anticipate that ClO₂ will react with compounds containing phenolic amino and thiol functional groups (Hoigne and Bader, 1994).

Ozonation. Ozone (O₃) is used in water treatment as both a disinfectant and an oxidant. During ozonation, two strong oxidants can lead to transformation of EDCs and PPCPs and other organic compounds: molecular O₃ and hydroxyl radicals (HO[•]) (Hoigne and Bader, 1983a, 1983b). O₃ is a selective electrophile that reacts with amines, phenols, and double bonds in aliphatic compounds, while HO[•] reacts less selectively with second-order rate constants (k_{HO}) on the order of 10⁶ to 10¹⁰ M⁻¹s⁻¹ (Buxton *et al.*, 1988; Haag and Yao, 1992). As a result of the selective nature of ozone, transformation of micropollutants may require the use of advanced oxidation processes (AOPs), such as UV/hydrogen peroxide (H₂O₂), O₃/H₂O₂, or UV/O₃ (Hoigne, 1998; Acero *et al.*,

2000; Acero and Von Gunten, 2001). Given information on water quality (e.g., alkalinity, pH, and NOM) it may be possible to estimate the concentrations of O_3 and OH present during ozone treatment. Such data can be used with second-order rate constants to predict the rate of transformation of EDCs and PPCPs during ozone treatment.

Preliminary data for a set of EDC/PPCP compounds indicate a wide range of reactivity for reactions with ozone; roxithromycin ($4.5 \times 10^6 \text{ M}^{-1}\text{s}^{-1}$), diclofenac ($>10^5 \text{ M}^{-1}\text{s}^{-1}$), ethinylestradiol ($>10^5 \text{ M}^{-1}\text{s}^{-1}$), carbamazepine ($0.78\text{--}3 \times 10^5 \text{ M}^{-1}\text{s}^{-1}$), sulfamethoxazole ($10^5 \text{ M}^{-1}\text{s}^{-1}$), bezafibrate ($590 \text{ M}^{-1}\text{s}^{-1}$), ibuprofen ($6 \text{ M}^{-1}\text{s}^{-1}$), diazepam ($0.95 \text{ M}^{-1}\text{s}^{-1}$), and ipramide ($<0.8 \text{ M}^{-1}\text{s}^{-1}$) (Huber *et al.*, 2002). Most k_{400} second-order rate constant values were on the order of $5 \times 10^5 \text{ M}^{-1}\text{s}^{-1}$. Under conditions encountered in water treatment systems ($[HO]/[O_3] \approx 10^{-8}$), only those compounds with ozone rate constants (k_{O_3}) greater than $\sim 50 \text{ M}^{-1}\text{s}^{-1}$ will be transformed to an appreciable degree ($>50\%$) through direct reactions with ozone. Therefore, during ozonation the mechanism of oxidation will be O_3 or a combination of O_3 and $HO^\bullet$. Some reports have documented the removal of EDCs and PPCPs in bench-scale treatment systems. For example, ozonation removed diclofenac, carbamazepine, and bezafibrate, but not clofibric acid (Sacher *et al.*, 2000). Improved removal of clofibric acid, ibuprofen, and diclofenac occurred when ozonation was conducted in the presence of hydrogen peroxide (0.4 to 0.7 mg H_2O_2 /mg ozone dosed) (Carlson *et al.*, 2000). Estrogen steroids and nonylphenols also reacted with ozone under conditions comparable to those encountered in water treatment systems (West, 2000). Ozonation of estrogenic chemicals in spiked groundwater indicated some removal of mestranol, estradiol, ethinylestradiol, norethistrone, ethistrone, and estril by aeration alone, and higher removals with applied ozone (Carlisle *et al.*, 1996). However, most EDCs and PPCPs have low Henry's Law constants, and aeration would not appear to be an effective means for removal. In separate work, a linear relationship between ozone dose and fraction of E2 remaining in model waters was apparently observed during O_3 and O_3/H_2O_2 processes (Kosaka *et al.*, 2000).

Ultraviolet (UV) irradiation. UV lamps are used widely for microbial disinfection of water and wastewater. In several cases, they also have been used for treatment of micropollutants (Mofidi *et al.*, 2000). Because several EDCs and PPCPs have chromophores that lead to adsorption of light at UV wavelengths, many may be amenable to transformation during UV treatment. However, typical UV doses required for disinfection (i.e., <5 to 30 mJ/cm^2) are several orders of magnitude lower than

those used for treatment of micropollutants. Therefore, UV treatment of EDCs and PPCPs probably will not be economically competitive with other advanced treatment methods (e.g., reverse osmosis). As discussed previously, UV treatment in combination with ozone or hydrogen peroxide may be practical in some situations.

UV alone or as part of AOP systems has been used to oxidize pesticides and other micropollutants, primarily in groundwater (Beltran *et al.*, 1992, 1993, 1996, 2000; Larson and Weber, 1994; Chiron *et al.*, 2000; De Laat *et al.*, 1999). Few reports of EDC or PPCP removal during UV treatment exist. For example, oxidation of fragrances (nitromusks) is achieved using UV light produced by low-pressure mercury lamps with faster transformation rates with the addition of hydrogen peroxide (Neamtu *et al.*, 2000). At UV doses of 3000 mJ/cm^2 , the removal of different antibiotics from distilled and natural waters ranged between 50 to 80% for the seven antibiotics, which were all selected because the compounds were detectable by HPLC.

Biotransformation

Biotransformation may provide a basis for the cost-effective removal of EDCs and PPCPs from water. Available data from municipal wastewater treatment systems suggest that many of the compounds are transformed by bacteria (Johnson *et al.*, 2000; Johnson and Sumpter, 2001; Termes *et al.*, 1999a, 1999b). However, little is known about the importance of biotransformation in drinking water treatment plants or in soil. Data from sites where wastewater effluent is used to recharge aquifers (i.e., soil aquifer treatment systems) indicate that many of the PPCPs are removed during the first few weeks of passage through the aquifer (Drewes *et al.*, 2001b). However, certain recalcitrant compounds including the antiepileptics, carbamazepine and primidone, and iodinated X-ray contrast media persist during infiltration through vadose and saturated soil zones (Drewes *et al.*, 2001a, 2001b). Similar results were observed in bank filtration (Heberer, 2002) and during slow sand filtration in drinking water treatment plants (Sacher *et al.*, 2000). These studies confirm that some PPCPs are biodegradable, while others are not or have not yet been investigated.

Membrane separation

Most organic EDC/PPCP compounds range from 150 to 500 Daltons in molecular size. As a result, only those compounds associated with particles or colloidal organic matter will be removed during microfiltration and ultrafiltration (UF). For example, microfiltration (0.1 to $0.4 \mu\text{m}$) did not remove two steroid hormones and six dif-

ferent acidic drugs and beta blockers at two different full-scale water recycling systems treating tertiary municipal wastewater effluent (Huang and Sedlak, 2001). Most EDCs and PPCPs will be removed by reverse osmosis (RO) and tight nanofiltration (NF) systems (i.e., those with a low molecular weight cutoff). For example, RO can achieve greater than 90% removal of steroid hormones (Huang and Sedlak, 2001).

Experience with other organic/inorganic compounds suggests that polar compounds and charged compounds that interact with membrane surfaces will be better removed than less polar or neutral compounds (Huxstep and Sorg, 1988; Durand *et al.*, 1992; Berg *et al.*, 1997; Carlson, 2000; Yoon *et al.*, 2001, 2002a, 2002b). For example, the removal efficiency of several low molecular weight compounds (~ 150 Daltons) increased at higher pH due to electrostatic repulsion between RO membrane and dissociated organic compounds (Ozaki and Li, 2002). In the same work, removal of neutral organic compounds increased linearly with molecular weight and molecular width. Hydrophobicity of the micropollutant and membrane also affect removal. For example, pesticide adsorption on, and removal by, RO and NF membranes was correlated with $\log K_{OW}$ (Kiso *et al.*, 2001a, 2001b).

Several recent laboratory studies also have demonstrated the removal of PPCPs from water. Compounds removed by RO included several different antibiotics (Adams *et al.*, 2002). Results from laboratory studies conducted by adding compounds to deionized water should be interpreted with caution because the presence of cations and NOM can alter removal efficiency. RO, NF, and charged UF membranes can remove inorganic EDCs (e.g., arsenic, perchlorate) (Uludag *et al.*, 1997; Urase *et al.*, 1997; Chianese *et al.*, 1999; Vrijenhoek and Waypa, 2000; Van der Bruggen *et al.*, 2001; Yoon *et al.*, 2002a). Overall, membrane separation provides an excellent barrier for most EDCs and PPCPs, except the lower molecular weight uncharged compounds.

SUMMARY OF WATER TREATMENT PROCESSES FOR EDC AND PPCP CONTROL

Table 2 provides a generalized summary of the potential for removal of various classes of EDCs and PPCPs. Estimates of removal are based upon chemical structure (size, hydrophobicity, functional group composition).

1. Coagulation would only be expected to remove hydrophobic compounds associated with particular or colloidal material with high organic carbon content.
2. Activated carbon adsorption removes hydrophobic

compounds very well, but competition between more polar or larger molecular weight compounds and other matrix organics has not been well documented.

3. Oxidation will preferentially attack compounds with electron-activating functional groups (thiols, amines, hydroxyl) located near C=C bonds (benzene rings). Organic compounds will react more rapidly with ozone than chlorine dioxide or chlorine.
4. Membranes provide a physical barrier capable of high removals, but removals are dependent upon compound structure (size, polarity) and membrane properties.

Given experience with removing pesticides and other trace micropollutants, water treatment technologies can be integrated into existing WTPs or designed into new facilities to assure high levels of EDC and PPCP compound removal. For example, simple process modifications such as addition of powder-activated carbon to a convention WTP during periods of high-risk of EDC or PPCP in the raw water (e.g., low streamflow during the summer comprised primarily of upstream wastewater discharge) could provide high levels of removal. Incorporation of more advanced technologies could require extensive modifications to WTP operations. For example, inclusion of O_3 or AOP systems should be followed by biofiltration to remove polar oxidation byproducts. Combinations of treatments may be required to remove mixtures of compounds that may occur in a raw drinking water (e.g., membranes, oxidation).

Future research needs

A great deal of additional data are needed to understand the relevance of trace EDCs and PPCPs in water and how these compounds may be removed by water treatment. It is important to gain more information as to the toxicological impacts of trace levels of EDCs and PPCPs in water. Once these impacts are quantified, safe exposure limits can be established that will allow the water industry to determine "good removal" rates. Standardized analytical methods for detection of commonly occurring EDCs and PPCPs are critical. These methods should be based on equipment that most laboratories could afford and have expertise to operate. Once analytical methodologies are available, environmental screening should include testing for bioaccumulation of EDCs in wildlife and humans. Future studies should seek to identify population-level impacts of EDCs and PPCPs on wildlife and relate these effects to biomarkers.

Although reports of EDC and PPCP removal by water treatment are beginning to become available, much is still unknown as to the fate of these emerging contaminants in WTPs. It is critical to understand the size dis-

tribution of EDCs and PPCPs and their association with particulate and colloidal materials in raw drinking water supplies to assess removal across conventional WTPs designed for particulate and colloidal removal. The oxidation capability of chloramines on EDC/PPCP compounds reactive with chlorine should be quantified. Oxidation byproducts should be identified and tested for both endocrine and carcinogenic health risks. Effects of nonionic polymers on improving EDC/PPCP removal during coagulation have not been reported. Aerobic biofilms should be compared to nonbiological sand filters to quantify the potential benefits of changing the point of chlorination in a conventional WTP to optimize EDC/PPCP removal. Breakthrough curves should be generated for GAC packed columns with a variety of EDC and PPCP compounds in water containing NOM to evaluate potential displacement/desorption of organics over time. Partition and permeation coefficients across membranes for EDCs and PPCPs should be determined. Additionally, membranes should be evaluated for leaching of plasticizers that may act as EDCs. Integrated water management options, which include source water protection, should complement advanced drinking water treatment.

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